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L2: Entry 3 of 3 File: USPT Sep 21, 1999

DOCUMENT-IDENTIFIER: US 5955475 A
TITLE: Process for manufacturing paroxetine solid dispersions

Brief Summary Text (54):
As used herein, the term "pharmaceutically acceptable salt" refers to derivatives of paroxetine wherein paroxetine is modified by making acid addition salts of the compound. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of the basic piperidine residue; and the like. The pharmaceutically acceptable salts of paroxetine include conventional non-toxic salts or quaternary ammonium salts, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethanesulfonic, ethanedisulfonic, oxalic, isethionic, and the like.

10019049/blessing

L10 ANSWER 7 OF 8 USPATFULL

ACCESSION NUMBER:	2001:162866 USPATFULL
TITLE:	Triglyceride-free compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S):	Patel, Mahesh V., Salt Lake City, UT, United States Chen, Feng-Jing, Salt Lake City, UT, United States
PATENT ASSIGNEE(S):	Lipocine, Inc., Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6294192	B1	20010925	
APPLICATION INFO.:	US 1999-258654		19990226	(9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Page, Thurman K.
ASSISTANT EXAMINER:	Channavajjala, Lakshmi
LEGAL REPRESENTATIVE:	Reed, Dianne E.Reed & Associates
NUMBER OF CLAIMS:	74
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:	3094

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to triglyceride-free pharmaceutical compositions for delivery of hydrophobic therapeutic agents. Compositions of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon dilution with an aqueous solvent, the composition forms a clear, aqueous **dispersion** of the surfactants containing the therapeutic agent. The invention also provides methods of treatment with hydrophobic therapeutic agents using these compositions.

L10 ANSWER 8 OF 8 USPATFULL

ACCESSION NUMBER:	2001:93131 USPATFULL
TITLE:	Solid carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S):	Patel, Mahesh V., Salt Lake City, UT, United States Chen, Feng-Jing, Salt Lake City, UT, United States
PATENT ASSIGNEE(S):	Lipocine, Inc., Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6248363	B1	20010619	
APPLICATION INFO.:	US 1999-447690		19991123	(9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Spear, James M.
LEGAL REPRESENTATIVE:	Reed, Dianne E.Reed & Associates
NUMBER OF CLAIMS:	57
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT:	3302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides solid pharmaceutical compositions for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or separately administered. In one embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compositions of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutrionals, cosmeceuticals and diagnostic agents.

L10 ANSWER 4 OF 8 USPATFULL

ACCESSION NUMBER:	2002:102031 USPATFULL
TITLE:	Compositions and methods for improved delivery of ionizable hydrophobic therapeutic agents
INVENTOR(S):	Chen, Feng-Jing, Salt Lake City, UT, United States Patel, Mahesh V., Salt Lake City, UT, United States
PATENT ASSIGNEE(S):	Lipocine, Inc., Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6383471	B1	20020507
APPLICATION INFO.:	US 1999-287043		19990406 (9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Bawa, Raj
LEGAL REPRESENTATIVE:	Reed, Dianne E., Reed & Associates
NUMBER OF CLAIMS:	114
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT:	3051

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a pharmaceutical composition including a hydrophobic therapeutic agent having at least one ionizable functional group, and a carrier. The carrier includes an ionizing agent capable of ionizing the functional group, a surfactant, and optionally solubilizers, triglycerides, and neutralizing agents. The invention further relates to a method of preparing such compositions by providing a composition of an ionizable hydrophobic therapeutic agent, an ionizing agent, and a surfactant, and neutralizing a portion of the ionizing agent with a neutralizing agent. The compositions of the invention are particularly suitable for use in oral dosage forms.

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:12137 CAPLUS
DOCUMENT NUMBER: 134:61565
TITLE: Solid and semi-solid formulations of paroxetine with increased stability and bioavailability
INVENTOR(S): Rosenberg, Joerg; Breitenbach, Joerg; Liepold, Bernd
PATENT ASSIGNEE(S): Knoll A.-G., Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19930454	A1	20010104	DE 1999-19930454	19990702
WO 2001001956	A2	20010111	WO 2000-EP5848	20000623
WO 2001001956	A3	20010712		
W: AU, BR, CA, CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1189614	A2	20020327	EP 2000-942125	20000623
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

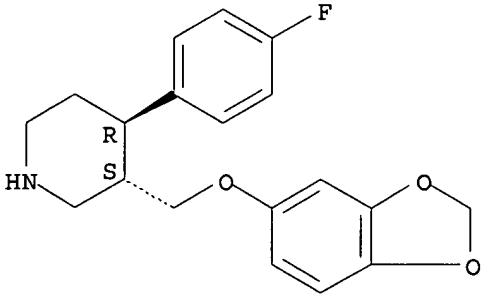
PRIORITY APPLN. INFO.: DE 1999-19930454 A 19990702
WO 2000-EP5848 W 20000623

AB The invention concerns solid and semi-solid formulations of paroxetine and its physiol. acceptable salts that contain the mol.-dispersed active substance in a matrix composed of a synthetic **polymer** with glass transition temp. > 90.degree.C. The invention also concerns the prepn. of the formulations. 80% Of the active substance is bioavailable within 30 min after dosage. Paroxetine or its salt is mixed and melted with the matrix material in the extruder, followed by the forming procedure. In another version paroxetine, **ammonium chloride** and matrix material are coextruded. The product is used for the prepn. of tablets. Thus 30 wt./wt.% paroxetine hydrochloride and 70 wt./wt.% copovidon (N-vinylpyrrolidone-vinylacetate copolymer 60/40) were processed in a twin-screw extruder at 145.degree.C. The product was used as for the formulation of tablets with the following compn. in wt./wt.%: paroxetine hydrochloride extrudate 38; microcryst. cellulose 15; calciumhydrogen phosphate 35; sodium-croscarmellose 10; highly disperse silica 1; magnesium stearate 1.

10019049/blessing

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 61869-08-7 REGISTRY
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, (3S,4R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, (3S-trans)-
OTHER NAMES:
CN (-)-Paroxetine
CN (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine
CN Aropax
CN BRL 29060
CN FG 7051
CN **Paroxetine**
CN Paxil
FS STEREOSEARCH
DR 63952-24-9
MF C19 H20 F N O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1197 REFERENCES IN FILE CA (1962 TO DATE)
24 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1199 REFERENCES IN FILE CAPLUS (1962 TO DATE)

100596398/blessing

DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19930454	A1	20010104	DE 1999-19930454	19990702
	WO 2001001956	A2	20010111	WO 2000-EP5848	20000623
	WO 2001001956	A3	20010712		
	W: AU, BR, CA, CN, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1189614	A2	20020327	EP 2000-942125	20000623
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	DE 1999-19930454	A	19990702		
	WO 2000-EP5848	W	20000623		

AB The invention concerns solid and semi-solid formulations of **paroxetine** and its physiol. acceptable salts that contain the mol.-dispersed active substance in a matrix composed of a synthetic polymer with glass transition temp. > 90.degree.C. The invention also concerns the prepn. of the formulations. 80% Of the active substance is bioavailable within 30 min after dosage. **Paroxetine** or its salt is mixed and melted with the matrix material in the extruder, followed by the forming procedure. In another version **paroxetine**, **ammonium chloride** and matrix material are coextruded. The product is used for the prepn. of tablets. Thus 30 wt./wt.% **paroxetine** hydrochloride and 70 wt./wt.% copovidon (N-vinylpyrrolidone-vinylacetate copolymer 60/40) were processed in a twin-screw extruder at 145.degree.C. The product was used as for the formulation of tablets with the following compn. in wt./wt.%: **paroxetine** hydrochloride extrudate 38; microcryst. cellulose 15; calciumhydrogen phosphate 35; sodium-croscarmellose 10; highly disperse silica 1; magnesium stearate 1.

=>

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 2002:977660 CAPLUS
DN 138:29184
TI A process for preparing paroxetine hydrochloride limiting formation of pink compounds
IN Avrutov, Ilya; Pilarski, Gideon
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002102382	A1	20021227	WO 2002-US19016	20020614
WO 2002102382	C2	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-298603P P 20010614
US 2001-326993P P 20011005
US 2002-346048P P 20020104

AB The present invention provides a process for prepg. **paroxetine** -HCl (I) from **paroxetine** base which provides I substantially free of pink-colored compds. or an impurity identified by an HPLC RRT of about 1.5. The processes utilize a buffer, a molar ratio of HCl to **paroxetine** base of <1, and crystallize/recrystallize in the presence of an effective amt. of an anti-oxidant. A preferred way to create a buffer is by using **ammonium chloride**. A preferred anti-oxidant is ascorbic acid. The present invention also provides for re-crystg. I prepd. by the above methods or any other methods in the presence of an effective amt. of an anti-oxidant such as ascorbic acid. A preferred solvent system for recrystn. is a mixt. of acetone and methanol. Processes of the present invention can combine these various features. An aq. soln. of **ammonium chloride** in water was added to a soln. of **paroxetine** base in toluene. The reaction mixt. was intensively stirred at ambient temp. while concd. HCl was added in such manner that the pH of the reaction mixt. stayed between 3.5 and 8. A ppt. formed which was filtered and then washed with toluene and water. The resulting material was dried at 60.degree. under vacuum to give I. The soln. did not develop a pink color after standing for 20 min.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 2001:12137 CAPLUS
DN 134:61565
TI Solid and semi-solid formulations of paroxetine with increased stability and bioavailability
IN Rosenberg, Joerg; Breitenbach, Joerg; Liepold, Bernd
PA Knoll A.-G., Germany
SO Ger. Offen., 4 pp.
CODEN: GWXXBX